Connecting via Winsock to STN

* * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:26:53 ON 20 MAR 2007

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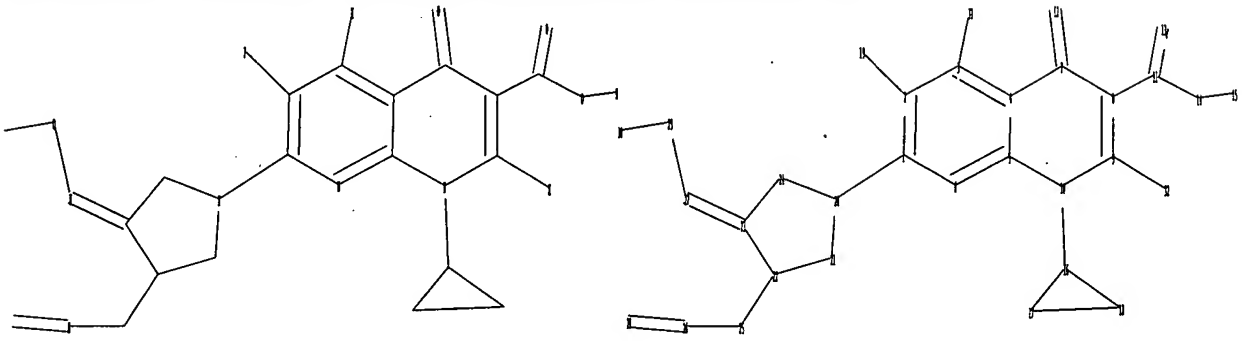
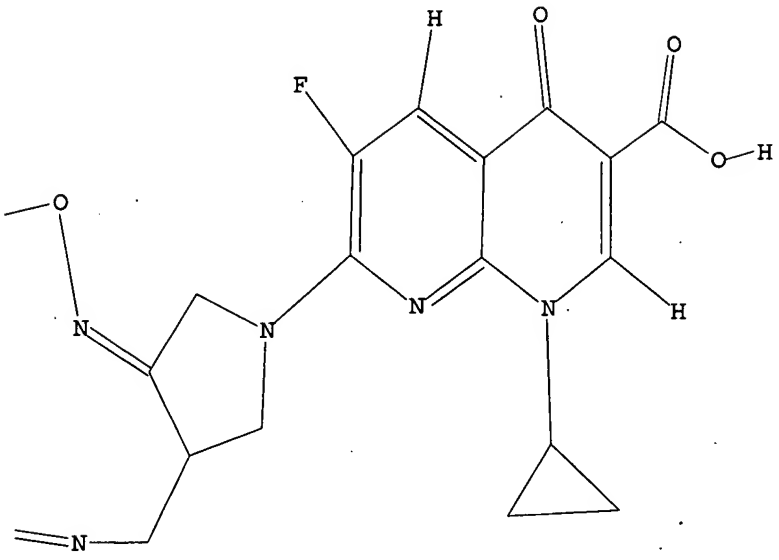


chain nodes :
11 12 13 14 15 19 25 26 27 28 29 30 31 32
ring nodes :
1 2 3 4 5 6 7 8 9 10 16 17 18 20 21 22 23 24
chain bonds :
1-20 2-19 3-31 7-12 8-11 9-32 10-16 11-13 11-14 14-15 22-25 23-27 25-26
26-28 27-29 29-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10 16-17 16-18 17-18 20-21
20-24 21-22 22-23 23-24
exact/norm bonds :
1-20 4-7 5-10 7-8 7-12 8-9 9-10 10-16 16-17 16-18 17-18 20-21 20-24
21-22 22-23 23-24 23-27 25-26 26-28 27-29 29-30
exact bonds :
2-19 3-31 8-11 9-32 14-15 22-25
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-13 11-14

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom 17:Atom 18:Atom
19:CLASS 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS
28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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=> s l1 full

L2 6 SEA SSS FUL L1

=> file ca

=> s l2
L3 1 L2

=> d ibib abs hitstr

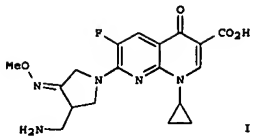
L3 ANSWER 1 OF 1 CA COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 139:337960 CA
TITLE: Improved two-step process for preparing acid salts of gemifloxacin via Schiff-base protected intermediates
INVENTOR(S): Choi, Hoon; Choi, Sang-Chul; Nam, Do-Hyun; Choi, Bo-Seung
PATENT ASSIGNEE(S): LG Life Sciences Ltd., S. Korea
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003087100	A1	20031023	WO 2003-KR683	20030404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2003080292	A	20031017	KR 2002-18847	20020408
CA 2481217	A1	20031023	CA 2003-2481217	20030404
AU 2003219581	A1	20031027	AU 2003-219581	20030404
EP 1497290	A1	20050119	EP 2003-715805	20030404
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009037	A	20050201	BR 2003-9037	20030404
US 2005148622	A1	20050707	US 2004-510514	20030404
CN 1649868	A	20050803	CN 2003-809548	20030404
JP 2005529112	T	20050929	JP 2003-584056	20030404
NZ 536174	A	20060929	NZ 2003-536174	20030404
NO 2004004629	A	20041027	NO 2004-4629	20041027
PRIORITY APPLN. INFO.:			KR 2002-18847 A	20020408
			WO 2003-KR683 W	20030404

OTHER SOURCE(S): CASREACT 139:337960; MARPAT 139:337960
GI

L3 ANSWER 1 OF 1 CA COPYRIGHT 2007 ACS on STN (Continued)



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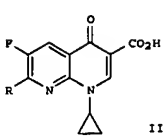

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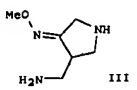
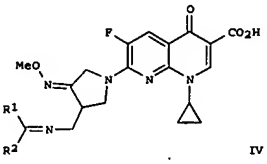


III



IV

AB The invention relates to a process for preparing acid salts of gemifloxacin (I), a known quinolone-type antibiotic agent having potent antimicrobial activity. The process provides advantages such as simplicity of process, improvement of productivity, improvement of yield, and the like, by reducing a conventional three-step process to two steps. More specifically, by using a Schiff base-protected intermediate as the product of the first step, and its concomitant hydrolysis during salt formation in the second step, a secondary amine byproduct is avoided, and the normal third step (recrystn.) can be omitted, leading to higher yields and purity. The claimed invention involves preparation of I·HA [HA = organic or inorg. acid] in two steps. In the first step, activated naphthyridine derivs. II react with (aminomethyl)pyrrolidine derivative salts III·2HX and carbonyl compds. R1COR2 in an aqueous and/or organic solvent in the presence of an organic base, to give Schiff base-protected intermediates IV [wherein: R = Cl, F, Br, iodo, MeSO2, p-MeC6H4SO2; X = Cl, Br, I, CF3COO, MeSO3, p-MeC6H4SO3, or HSO4; R1, R2 = H, (un)saturated (cyclo)alkyl, aromatic group optionally substituted by alkyl, alkoxy, OH, cyano, or halo; or R1R2 form a ring]. In the second step, treatment of IV with acids HA in an aqueous and/or organic solvent gives simultaneous deprotection and salt formation to yield I·HA. Six examples of the first step, and two examples of the second step are given. In the first step, the preferred carbonyl

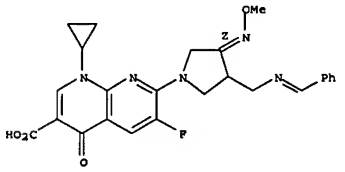
L3 ANSWER 1 OF 1 CA COPYRIGHT 2007 ACS on STN (Continued)

compd. is benzaldehyde, in terms of cost and stability. The preferred temp. range is 20-30° in view of reaction rate, yield, and purity. The preferred base is Et3N in terms of cost and yield. High-purity IV may be produced in > 90% yield. In the second step, the preferred solvent is aq. isopropanol in view of yield and purity. The most suitable acid HA is MeSO3H, and the preferred temps. are 40-50° for addn. of the acid, and 0-20° thereafter. Compared to the prior art, yields of I·HA are increased from about 65% to ≥ 80%. The process can also be applied to other quinolone antibiotics with atructures aimilar to that of I. For instance, reaction of III·2MeSO3H in aq. MeCN at 0-5°, first with PhCHO and Et3N, and then with II (R = Cl), followed by warming to room temp., gave IV (R1 or R2 = Ph; other = H) in 94.8% yield on a 320-g scale. Hydrolysis of the latter in aq. iso-PrOH by dropwise addn. of MeSO3H at 40-45°, followed by cooling and seeding, gave I.MeSO3H in 95.1% yield.

IT 616827-43-1P, 7-[3-[(Benzylideneamino)methyl]-4-((Z)-methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid 616827-48-6P, 7-[3-[[(2-Chlorobenzylidene)amino]methyl]-4-((Z)-methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid 616827-56-6P, 7-[3-[[(2-Hydroxybenzylidene)amino]methyl]-4-((Z)-methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid 616827-63-5P, 7-[3-[[(4-Cyanobenzylidene)amino]methyl]-4-((Z)-methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid 616827-70-4P, 7-[3-[[(4-Methoxybenzylidene)amino]methyl]-4-((Z)-methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid 616827-77-1P, 7-[3-[[(1-Naphthylmethylene)amino]methyl]-4-((Z)-methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; improved preparation of gemifloxacin acid addition salts via Schiff base-protected intermediates)

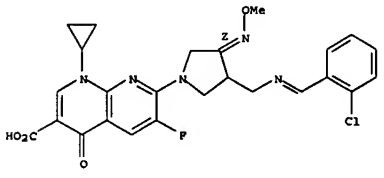
RN 616827-43-1 CA
CN 1,8-Naphthyridine-3-carboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(3Z)-3-(methoxyimino)-4-[[(phenylmethylene)amino]methyl]-1-pyrrolidinyl]-4-oxo- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



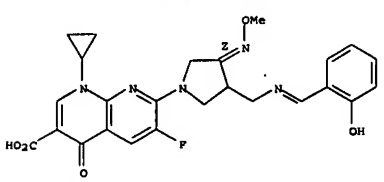
RN 616827-48-6 CA
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[(4Z)-3-[[[(2-chlorophenyl)methylene]amino]methyl]-4-(methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

Double bond geometry as deacribed by E or Z.



RN 616827-56-6 CA
CN 1,8-Naphthyridine-3-carboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4Z)-3-[[[(2-hydroxyphenyl)methylene]amino]methyl]-4-(methoxyimino)-1-pyrrolidinyl]-4-oxo- (9CI) (CA INDEX NAME)

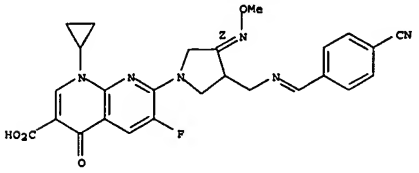
Double bond geometry as described by E or Z.



RN 616827-63-5 CA

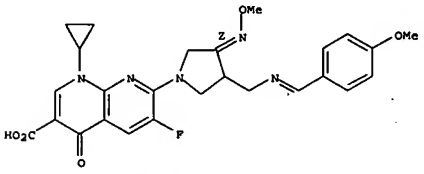
L3 ANSWER 1 OF 1 CA COPYRIGHT 2007 ACS on STN (Continued)
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[(4Z)-3-[[[(4-cyanophenyl)methylene]amino]methyl]-4-(methoxyimino)-1-pyrrolidinyl]-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



RN 616827-70-4 CA
CN 1,8-Naphthyridine-3-carboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(3Z)-3-(methoxyimino)-4-[[[(4-methoxyphenyl)methylene]amino]methyl]-1-pyrrolidinyl]-4-oxo- (9CI) (CA INDEX NAME)

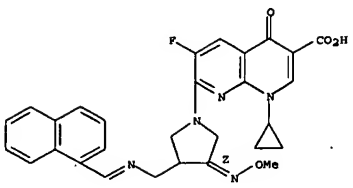
Double bond geometry as described by E or Z.



RN 616827-77-1 CA
CN 1,8-Naphthyridine-3-carboxylic acid, 1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(3Z)-3-(methoxyimino)-4-[[(1-naphthalenylmethylene)amino]methyl]-1-pyrrolidinyl]-4-oxo- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

L3 ANSWER 1 OF 1 CA COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/510,514

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     FILE 'REGISTRY' ENTERED AT 11:27:09 ON 20 MAR 2007
L1              STRUCTURE UPLOADED
L2            6 S L1 FULL

     FILE 'CA' ENTERED AT 11:28:38 ON 20 MAR 2007
L3            1 S L2

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---Logging off of STN---


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Executing the logoff script...


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STN INTERNATIONAL LOGOFF AT 11:29:18 ON 20 MAR 2007
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